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PRINCIPAL INVESTIGATOR: James R. Hebert, Sc.D

CONTRACTING ORGANIZATION: University of South Carolina
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13. ABSTRACT (Maximum 200 Words)

Conventional breast cancer(BrCA)risk factors explain 50% of variability in disease rates and change in incidence over time. The past two generations of American women have experienced major changes in physical activity, preparing and eating food, and increases in the prevalence of overweight. These factors may exert powerful influences on physiologic processes leading to cancer. This case control study aims to investigate the relationship between physical activity, diet, and adult weight history and breast cancer. Our goal is to recruit 648 incident cases of breast cancer and up 2 controls per case from the Breast Care Centers of the Palmetto Richland and Baptist Hospitals of Palmetto Health /South Carolina Cancer Center (BCC) - services that see a total of about 35,000 mammography screenees each year and in which about 700 women are diagnosed with breast cancer. After obtaining permission from the Human Use Review Office of the USAMRAA (on 30 November 2000) to begin recruitment we finished the run-in process and began recruitment in the Baptist Hospital BCC in spring of 2001. Recruitment at Richland began in May 2002. As of July 31, 2004, we had recruited 1203 subjects.

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breast cancer, diet, physical activity, body weight, psychological factors, epidemiology, case-control study

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Introduction:

It is clear from epidemiological studies that environmental factors are largely responsible for differences in breast cancer rates across populations and changes in U.S. rates over time. Dietary factors and those related to physical activity may have powerful influences on adult weight gain and several physiologic processes that could lead to cancer. However, obtaining unbiased self-reports of these behaviors is difficult, in part because they are subject to systematic reporting errors, such as recall and social desirability biases. This case-control study is measuring diet, adult weight history, and physical activity in women undergoing a diagnostic evaluation for potential breast cancer, but prior to diagnosis. The focus will be on two main suspects in breast cancer: consumption of fat as a factor that could be associated with increased risk; and certain fruits, vegetables, and grains containing high concentrations of functional constituents (phytoestrogens, antioxidants, protease inhibitors, indole glucosinolates) that may be protective. High levels of adult weight gain and physical inactivity, both of which may be related to increased risk, will be examined both as potential confounders to the diet exposures as well as independent predictors of breast cancer risk. The unique design of this case-control study provides a way to measure diet and other self-report measures before they can be affected by a woman's knowledge of whether or not she has breast cancer. We expect that a total of about 13,000 women will receive routine mammography for the first time in the Breast Care Center at the Palmetto Richland Memorial Hospital Campus of the Palmetto Health Alliance/South Carolina Cancer Center (BCC) over the 48-month recruitment period. Of these, about 5,400 will have confirmation by advanced diagnostic techniques, and about 20% of these will have histologically confirmed breast cancer. We project that 60% of women coming in for advanced diagnostic techniques (N=3,240 women [20-80 yrs]), will be willing to participate, of whom one-fifth (n=648) will have primary breast cancer. Age-, clinical system (i.e., Richland vs. Baptist)-, and time-matched controls will be obtained from the remaining disease-free women who visit the respective clinical sites within 3 weeks of the time that her matched case (i.e., women with breast cancer) enters the clinical system. Results from this investigation will add to our body of knowledge of the modifiable behaviors that are associated with incident breast cancer.

Specific Aims:

Using information from recently completed studies on sources of bias in assessment of dietary intake, this study will attempt to reconcile discrepancies between results of laboratory animal studies and cross-national comparisons strongly implicating diet as a cause of breast cancer and those from conventional epidemiologic studies that are much more equivocal on this topic. It will account for a number of covariates, especially physical activity and adult weight gain. The purpose of the proposed research is to test whether a dietary pattern associated with high-fat (generally salty or sweet) foods increases risk whereas a pattern emphasizing whole grain and vegetable intake decreases risk. This study is designed with full recognition that dietary variables are collected using assessment methods that are seen by subjects as "tests" and, therefore, are susceptible to psychological factors that are known to affect individuals in test-taking situations. Because secondary prevention will remain an important issue for the foreseeable future, it is also important that assessed populations be accessible and amenable to follow up to determine which, if any, dietary factors may be predictive of prognosis among those diagnosed with breast cancer and to increase disease risk among those found to be free of disease at baseline. The faculty and staff of the Breast Clinic, from which all cases and the clinic-based controls will be obtained, have a keen interest in the research potential of the clinic. Given high rates and thoroughness of patient follow-up, the clinic also presents excellent opportunities to investigate the natural history of breast cancer prognoses and to follow up breast cancer patients.

The primary goal of the proposed research is to investigate the role of diet and adult weight gain, with historical levels of activity being obtained to "characterize prior activity" to use as an adjustment for confounding in the etiology of breast cancer. The secondary goal of the research

will be to assemble cohorts of disease-free, high-risk women and breast cancer patients to: 1. establish breast cancer risk factors in women at high risk because of either a family history of the disease or presence of a precancerous lesion (i.e., women determined not to have breast cancer at the time of enrollment); and 2. delineate lifestyle, psychosocial and/or treatment factors that might affect prognosis in women with a histologically confirmed cancer of the breast, as we have done previously [1, 2].

Work Accomplished:

The approved Statement of Work (see Appendix 1) categorized the work objectives for the project into 4 discrete tasks, each with indications for the months from the study timeline in which these tasks will be accomplished. Due to unforeseen delays in getting Human Subjects approval from the Institutional Review Boards of the three bodies governing this research [(i.e., U.S. Army, University of South Carolina, and the Palmetto Health Alliance (now Palmetto Health)], the original study timeline has beenwas revised. The original timeline started in July 2000 (month 1) and participant recruitment was scheduled to begin in January 2001 (month 7). Final approval from all three institutions was not obtained until late February 2001, with recruitment beginning at Palmetto Baptist in the spring of 2001 and at the Richland Hospital campus of Palmetto Health in the spring of 2002. Full-scale recruitment at Richland is anticipated began with the post-vacation flow of work in September 2002.

With improvements in diagnostic procedures and concomitant reductions in the interval between first contact with the clinical system and diagnosis, we have had to modify our study design as described below. The recruitment is now proceeding well, though not at the pace originally envisaged. As a consequence of the design change, we have taken the opportunity to begin looking at the existence of bias in reporting health-related behaviors and will use these data in formal testing of study hypotheses, as we have done in previous work in BrCA studies. Differences in BMI (kg/m^2) of enrollees vs. screenees (but not cases vs. controls) indicate selection bias in overall enrollment into the study. Although it is too early to make strong inferences based on data collected, we have observed results confirmatory of other studies (i.e., higher breast cancer rates in the more educated and in Whites). Higher likelihood of BrCA in widowed women and lower likelihood in divorced and separated women are intriguing. Results indicating protection with more vigorous physical activity outside of the home and with more household activity are also consistent with those observed in other studies. There appear to be some differences emerging in terms of intakes of specific food groups, which will need to be monitored. Initial results on the DNA from buccal cells indicates sample adequacy.

In the following sections, each individual sub-task outlined in the Statement of Work (Appendix 1) is indicated in bold text and by a an alphabetic indicator (e.g., a, b, c,...). Our work to accomplish these sub-tasks follows in bulleted form. Where applicable, problems encountered in completing tasks are described and our plans for overcoming these barriers are outlined.

Task 1: Run-in Phase, Months 1-6 (July-December 2000):

a) Review baseline lifestyle and demographic questionnaire for completeness and for content validity.

- An initial Baseline questionnaire was complied (Appendix 2) and included the following sections
  - Demographics
  - Food Frequency Questionnaire
  - Physical Activity Assessment (Lifetime, Past-Year)
  - Medical/Family History
  - Personal Reaction Inventory (also known as the Marlowe Crowne Social Desirability Scale)
  - Martin-Larsen Approval Motivation scale (to measure social approval)
  - SF-36 Quality of Life

b) Revise baseline questionnaire as necessary.

- During questionnaire development phase, considerable refinement was made to several aspects of the baseline questionnaire in order to meet the objectives of this investigation and provide additional information about modifiable risk factors for breast cancer not specifically outlined in the original application (as secondary analyses)
  - The scope of the original FFQ was expanded to measure more effectively vegetable and fruit consumption in enough detail to evaluate specific dietary hypotheses
  - Two Physical Activity Assessments were adapted for self-administration
  - Sections on medical and family history were lengthened to support further research into the impact of sleep patterns, non-steroidal anti-inflammatory drugs, and various lifestyle factors on breast cancer development
- Ten clinic nurses pilot tested the baseline questionnaire in order to check for readability and relevance, as well as to assess the feasibility of administering a lengthy instrument to study participants.
- Pilot questionnaire data were also used to test questionnaire scanning software and SAS programming files. Data quality also was assessed from these pilot data.

c) Hire and train the Research Assistant.

- We currently employ two part time graduate assistants (1 PhD and 1 Masters candidates) and 1 assistant to recruit, collect data in the field and for data management tasks.
- A Data Manager is currently overseeing all aspects of data processing.

d) Develop a Manual of Operations (MOP), a detailed document describing data management systems.

- The MOP has been completed: and revisions were made as needed. (None required during this reporting period)

- The MOP's content is based on our successful experience with other large-scale epidemiologic studies, and describes how SAS, Teleform (optical scanning software), Excel, EpiInfo and other data management/tracking software are effectively integrated to manage and analyze the data.
- A Coding Manual was compiled and checked for accuracy.
- Standard Operating Procedures were developed to ensure that; participants are effectively and ethically recruited; high quality data are collected during the patient visits, and that data are efficiently and accurately entered for analysis.
- Security measures have been implemented to protect all participant information.

e) Develop and pilot test the participant tracking database, as well as all measurements and documenting procedures.

- A participant-tracking database has been constructed and is functioning in support of our recruitment and monitoring efforts.

f) Train staff in all data-related and clinic-based procedures.

- Staff is retrained on a regular basis to ensure quality data management and optimal procedures for participant recruitment, clinical measurements, and security.

Task 2: Recruitment, Months 7-48:

a) Of the 5,400 women visiting the Breast Care Center at the Palmetto Richland Memorial Hospital Campus of the Palmetto Health Alliance/South Carolina Cancer Center (BCC) for an advanced diagnostic work-up to rule in or rule out breast cancer, enroll 60% (3,240 women) as participants for the study.

As noted in the introduction, due to changes in regulations and the clinical system, it has been necessary to modify the recruitment strategy over time. We currently have settled on Strategy #3 as the final one that will be used for the duration of the study. We provide the three options considered as a permanent note for the record.

Strategy #1

Patients entering the clinical system for a screening mammogram were asked to complete a consent for telephone contact. Approximately 20% of the women were asked to return to the clinic for a diagnostic work-up for positive radiographical findings. Those patients who had agreed to contact upon screening were contacted and asked to participate.
Problems: Only 1/3 of patients who were scheduled for diagnostic work-up were referred from screening. The other 2/3 were patients referred by family physicians or Ob/Gyn physicians for suspicious symptoms (i.e. palpable mass). These patients did not have the opportunity to sign the consent for contact.

Strategy #2

Instead of telephone contact, we recruited participants as they waited for their diagnostic appointment in the clinic. No consent would be needed to talk with patients about their participation.
Problems: Although the response was positive, we were dependent upon the waiting time at the clinic. For instance, if the schedule was heavily booked, wait times were increased and participation increased. With less waiting time, patients were less inclined to participate. Other patients indicated that they would like to participate, but could not make a decision at that time because of anxiety associated with a diagnostic work-up. We also discovered that case recruitment did not meet expectations based upon clinic statistics. Thus providing further evidence that the anxiety associated with the appointment was preventing study participation.

Strategy #3
With improvements in diagnostic procedures and concomitant decreases in waiting time, most patients were completing the survey aware of their breast cancer status. Thus, the recall bias that we had hoped to avoid with the original study design was not possible. This necessitated the latest change in which cases and controls would be recruited via different clinical routes. Because of these changes in practice patterns, it was determined that we could go somewhat farther "downstream" to the oncology practice. Virtually all oncologists in the Midlands (the catchment area for the three tertiary care facilities serving the central portion of the state) practice out of South Carolina Oncology Associates (SCOA). Currently, SCOA has offices in each of the hospitals. At the end of 2003, they moved to a single practice site, which is centrally located in relation to the hospitals. Patients receive all outpatient treatment at this site.

In order to increase the accuracy of data collected, 2/3 of the questionnaires are administered by study personnel. This has assisted with retention of study participants by lessening the amount of time the participants had to spend completing the questionnaire at home. By using this method, more participants on average are completing the study and the participants are completing in a timely manner. Participants are mailed the demographics portion of the questionnaire and complete it at home. When they come in for their clinic appointment to have their measurements taken, study personnel administer the food frequency portion. The study personnel then call the participants and administer the physical activity portion over the phone during a scheduled call.

Cases: are now recruited within 6 months of diagnosis. Places of contact for recruitment of breast cancer cases are the hospital tumor registry, oncologist office, breast health nurse, surgical service, and radiation oncology. We receive monthly downloads from the largest patient pool, the Cancer Data Management Department (Tumor Registry), which accounts for approximately 80% of breast cancer diagnosis in the metropolitan Columbia area.

Controls: Because recruitment at the diagnostic appointment was not proving to be the optimal time to approach patients for participation, we will recruit controls via telephone recruitment after a screening or diagnostic appointment. Both mammography clinics will obtain a consent for contact from all patients coming to the clinic for either a screening mammogram or

diagnostic work-up. Those consenting to contact are placed in a database for telephone contact. Controls will be matched to cases on the hospital/clinic at which they were originally seen.

b) Using instruments described in section 4.2., collect data on: diet, physical activity, and other aspects of lifestyle; demographic variables; family and personal health-related history; and social desirability and social approval.

- Of the 1203 participants agreeing to participate and to whom questionnaires were provided, 637 participants have returned the questionnaires. A protocol is in place to follow up with participants who have not returned questionnaires.

c) Collect and bank pre-diagnostic blood, urine, and buccal and breast tissue samples among a subset for future molecular epidemiologic analyses and biochemical validation of dietary assessment procedures, to be funded by future ancillary projects.

- Isolation and purification of genomic DNA from buccal cells was carried out on samples of seven patients, which were randomly chosen.

- The technique used was the phenol-chloroform extraction method for purification of DNA. Polymerase chain reaction (PCR) was used to amplify genomic DNA and agarose gel electrophoresis performed. The gel showed the presence of DNA, but since we were not specifically looking for any nucleic acid sequences the PCR technique was used just to confirm the presence of DNA in the samples.

- The collection method of DNA was found to be effective in getting substantial amount of DNA after PCR. The samples were stored in 70% ethanol. Changes in storage procedures like change in storage vials, processing with EDTA and then storing for future use in 70% ethanol is recommended, for efficient processing and isolation of DNA.

d) Take anthropometric measurements, as described in section 4.3.

- 87% of participants recruited have had anthropometric measurements taken.

e) Abstract medical records for relevant health history and pathology data.

- As part of the new recruitment procedures, we obtain monthly downloads from the Cancer Data Management department (Tumor Registry) that includes the pathology section of the medical record, patient identifiers (for linkage), and other relevant data.

Task 3: Data Entry, Verification, and Interim Analyses, Months 7-48:

a) Flag all outlier and illogical responses.

- Most of the questions in the PWHS questionnaire require that the study participant fill in the bubbles with pencil. There are a few questions that require them to write numbers (for

recalled previous weight, height, etc). Once the questionnaires are received from the study participants the study staff look for any stray pencil marks that may cause incorrect values to be output when they are scanned. After this check and making corrections if any, the questionnaires are scanned using the Teleform software. A verification process is built into the software that allows the study staff to verify the scanned data with the actual questionnaire. After the verification process is completed the software outputs the data into a 'Comma Separated Value' (CSV) file.

- Towards the process of creating an analytic dataset SAS programs have been written to read these CSV files and to look for errors in the data. Multiple programs have been written to check individual sections of the questionnaire. The program written to read in the measurements collected in the clinic checks for extreme values of height, weights, and other body measurements. If any extreme values are detected the study staff check the actual clinic form to verify and correct the information if there is an error. Once the clinic data has been checked and any errors corrected the data is output into an analytic dataset. As participants are enrolled into the study the same process is followed and the data is appended to the original dataset.

- SAS programs have also been written to check for consistency of the physical activity data collected in the questionnaires. These programs calculate the number of hours a participant has spent in a certain category of activity per day. Similarly programs have been written to identify outliers in the Food Frequency Questionnaire (FFQ). The program calculates the number of servings of the different food groups (based on USDA recommendations) and looks for outliers in these data.

- We send the participants a report with results based on their clinic measurements and on the physical activity data.

b) Verify all outlier and illogical responses, re-contacting participants, if necessary.

- Up until this point we have not encountered any critical errors that has required us to re-contact the participants.

c) Conduct simple descriptive analyses (e.g., cross-tabulations and univariate statistics).

- An interim analysis has been completed as of July 31, 2003. See appendix.

d) At months 13, 25, and 37 conduct multivariable analyses, as described in section 4.8. of the proposal.

- All previous sections (a, b, c) have been implemented in order to prepare for this task.
- As above, we are too early in the recruitment process for this task to be completed, at least in terms of formal hypothesis testing. However, as noted we have conducted descriptive interim analyses as of July 31, 2003.

Key Research Accomplishments:

Currently, we have been collaborating with Palmetto Health on the design and implementation of a research database and utilizing their cancer data management system to its fullest potential. As the result of recent HIPAA guidelines, we have developed and implemented a research database that will greatly benefit this study as well as future studies. In this process, we have developed an optically scannable pre consent form, which greatly decreases staff effort on data entry and increase data accuracy.

Reportable Outcomes:

Study products: There have been a considerable number of data collection instruments and recruitment and informational materials that have been produced in the first year of the study (see appendices). As no such study has been attempted in South Carolina previously, the existence of these instruments and materials has far-reaching implications. Additionally, each patient is given a report of her anthropometric, physical activity, and dietary data along with an explanation of what these values mean. We also are planning to write a paper with the Cancer Data Management department team on recruitment of cases through their rapid ascertainment system.

Funding applied for and received based on this award:

Our Clinical Sciences Studies Liaison, Swann Adams (Doctoral Candidate) was recently funded for her grant entitled "Physical Activity and Hormone Receptor-Defined Breast Cancer" by the American Colleges Sports Medicine Paffenbarger Grant.

A Co-Principal Investigator, Dr. Joan Cunningham, was awarded a grant by the South Carolina Research Initiative entitled "Cancer Prevention Drug Discovery for Breast and Colon Cancer".

Training opportunities: there currently are two graduate assistants (1 doctoral and 1 masters student in the Department of Epidemiology and Biostatistics at the Arnold School of Public Health) who are working on various aspects of this study.

Planned applications?
1) Follow-up QOL and body composition outcomes at 12- and 24-months, post-diagnosis
2) Follow-up recurrence?
3) Physical Activity and Hormone Receptor-Defined Breast Cancer

References:

1. Hebert JR, Hurley TG, Ma Y. The effect of dietary exposures on recurrence and mortality in early stage breast cancer. Breast Cancer Res Treat 1998;51:17-28.
2. Hebert JR, Augustine A, Barone J, Kabat GC, Kinne DW, Wynder EL. Weight, height and body mass index in the prognosis of breast cancer: early results of a prospective study. Int J Cancer 1988;42:315-318.

Appendices:

A.1. Approved Institutional Review Board Consent Form

PALMETTO HEALTH ALLIANCE

IRB #2000-69
(No samples required)

INFORMED CONSENT TO PARTICIPATE IN RESEARCH

TITLE: QUASI-PROSPECTIVE STUDY OF BREAST CANCER AND DIET

PRINCIPAL INVESTIGATOR: James R. Hebert, Sc.D.

ADDRESS: Department of Epidemiology and Biostatistics
University of South Carolina
School of Public Health
Columbia, SC 29208
Phone: 803.777.7666

SUBJECT'S NAME: _____ **DATE:** _____

SPONSOR: United States Department of Defense

INVITATION TO TAKE PART AND INTRODUCTION:

You are invited to volunteer for a research study. This form is designed to provide you with information about the study and to answer any questions that you may have. You have been asked to be in this study because you have recently been scheduled for a visit for diagnostic services at one of the hospitals within the Palmetto Health Alliance (Columbia, S.C.).

PURPOSE OF THE RESEARCH:

The main purpose of this study is to investigate the relationship between diet and physical activity levels and breast cancer risk. While much has been written about diet and breast cancer, results of research studies have produced inconsistent results in relating health related behaviors to breast cancer.

YOUR RIGHTS: It is important for you to know that:

- YOUR PARTICIPATION IS ENTIRELY VOLUNTARY.
- YOU MAY DECIDE NOT TO TAKE PART OR DECIDE TO QUIT THE STUDY AT ANY TIME.
- YOU WILL BE TOLD ABOUT ANY NEW INFORMATION OR CHANGES IN THE STUDY THAT MIGHT AFFECT YOUR PARTICIPATION.
  THE QUALITY OF CARE YOU RECEIVE AT THE HEALTH CENTER WILL NOT BE AFFECTED IN ANY WAY IF YOU DECIDE NOT TO PARTICIPATE, OR IF YOU WITHDRAW FROM THE STUDY.

PROCEDURES:

We will be asking you to complete a questionnaire packet that contains questions about several topics such as your education, job, date of birth, and the age(s) of your children, if any.

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Subject's Initials_____

03-19-2004 - 03-18-2005

Additionally, we will ask you to indicate the types and amounts of foods you typically eat, as well as your body weight and physical activity levels throughout your life. This questionnaire packet will require up to 2 hours to complete. It consists of six different questionnaires ranging from 1 to 19 pages. We have selected questionnaires that have been used in other national studies and found to be acceptable to a wide range of individuals. Despite this, you are not required to answer questions that you do not feel comfortable answering.

In addition to completing the questionnaire packet, we will ask you to visit our offices located in or near the breast clinic for about 30 minutes in order to complete additional measurements. For most people, they will prefer to do this while they wait for their clinic appointment; however, it can be scheduled on another day more convenient to you. If we do not complete your measurements before you are called to your breast clinic appointment, you may stop by the office after your appointment to complete the appointment.

During this visit, we will measure your weight, height, the circumference of your hips and waist (with a tape measure), and your body composition (using bioelectrical impedance). For the bioelectrical impedance measurements, we will ask you to lie down for about 5 minutes. Research personnel will place two electrodes on your hand and two on your feet. There is no risk of electrical shock and you will not feel the measurement being made. If, **as a part of your routine medical care**, you are scheduled for or have had a diagnostic breast biopsy, we will obtain a small portion of the biopsy tissue for this research study. No extra breast tissue will be taken during the biopsy for the purposes of this research study, and the small amount donated for this research will not interfere in any way with your medical care. **This only allows us to utilize breast tissue that your doctor will take or has already taken as a part of his/her normal care for you-a breast biopsy will not be done just for this study.** The biopsy material obtained for this research study may be used to determine enzyme levels that are important in regulating levels of female hormones (estrogens).

ALTERNATIVES:

You may choose to not take part in this study. If so, you would not have to do any of the things listed above that pertain to this research study. As a part of your medical care, you may still be asked to undergo a breast biopsy. Your decision not to take part in this study will not affect your medical care in any way.

RISKS AND INCONVENIENCES:

There is minimal risk or discomfort when we measure your weight, height, arm skin thickness, waist and hip circumferences, or body composition using bioelectrical impedance. There is minimal risk in answering any of the study questions.

All results obtained as part of this research will remain confidential. When we do the statistical analyses for the entire study we will not reveal your identity or the identity of anyone else in the study.

Subject's Initials_____

COMPENSATION IN CASE OF INJURY:

All forms of medical diagnosis, treatment and research, whether routine or experimental, involve some risk of injury. In spite of all precautions, you might develop complications from participation in this study. In the event of any injury resulting directly from the research procedures, neither the study personnel, the University of South Carolina, nor the Palmetto Health Alliance have made any provision for the payment of any financial compensation to you or to provide any financial assistance for medical or other costs.

This study is being funded by the Department of Defense and conducted by the United States Army in conjunction with the University of South Carolina. Army regulations provide that, as a volunteer in a study conducted by the United States Army, you are authorized all necessary medical care for any injury or disease that is a direct result of your participation in the research. The Principal Investigator or his designee will assist you in obtaining appropriate medical treatment under this provision, if it is required. If you have any questions concerning your eligibility for Army-funded medical treatment you should discuss this issue thoroughly with the Principal Investigator or his designee before you enroll in this study. This is not a waiver or release of your legal rights.

BENEFITS:

This study may be of no direct benefit to you. However, we will make study results available to you when it is feasible for us to do so. At the end of the study, you may request a summary of all of your own results with a brief description of what they mean. As results from the entire study are published, we will advise you and you may request copies of these as well. Additionally, the knowledge gained from your participation in this research may help further our understanding of how to prevent or treat breast cancer.

COSTS:

There will be no direct cost to you for participating in the study.

REMOVAL FROM STUDY:

You may be taken out of the research study if it appears that you are unable to keep your appointment, provide cheek or urine samples, or do not provide valid answers on the questionnaires. If this occurs, you will be given a full explanation for your removal.

CONFIDENTIALITY:

Your research records will be confidential to the extent possible by law. In all records of the study a code number will identify you and only the researchers will know your name. Your name will not be used in any reports or publications of this study. Your discussions with anyone who works on this study will be kept confidential, with two exceptions. We are compelled by law to inform an appropriate other person if: (1) we hear and believe that you are in danger of hurting

Subject's Initials

yourself or someone else, or (2) if there is reasonable suspicion that a child, elder, or dependent adult has been abused.

FUTURE CONTACT:

Cancer research proceeds in stages, and questions may develop that are presently unknown to us. We may want to ask you to participate in a follow-up breast cancer study at some point in the future. If this occurs, the reasons for your eligibility and the purposes of the follow-up study will be clearly described to you. You have a right to accept or decline participation in future studies should we contact you.

PATIENT PROTECTION:

Further information on the research to be performed, or regarding the risks and benefits of participation, or alternative treatments may be obtained from James R. Hebert at 803-434-6009. This study has been approved by the committee to protect human rights for the Palmetto Health Alliance. Information concerning your rights as a research subject can be obtained by contacting the Office of Corporate Counsel at (803) 296-2124.

Should you be injured as a direct result of participating in this research project, you will be provided medical care, at no cost to you, for that injury. This will entail billing your insurance provider. You will not receive any injury compensation, only medical care. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the principal investigator before you enroll in this study.

Subject's Initials_____

PALMETTO HEALTH ALLIANCE

IRB #2000-69
(No samples required)

Title: QUASI-PROSPECTIVE STUDY OF BREAST CANCER AND DIET
P. I. Name: James R. Hebert, Sc.D.

I have read the informed consent to participate in a research study or it was read to me by: _____. Anything I did not understand was explained to me by: _____, and any questions I had were answered by: _____

I certify that I am / am not [circle one] participating in another research project at this time, and have discussed the implications of such activity with the project director(s) of this project and/or my physician.
During this study, I have been asked to answer questions about my diet, weight history, and physical activity, and to donate a portion of my breast biopsy for breast cancer research (only if applicable). In addition, I have been asked to allow body composition measures to be made (height, weight, circumference measures, and bioelectrical impedance measures). There is a chance that the information and biological samples donated to this study may be used in other research studies and may have some commercial value. No commercial value is anticipated at this time. Should donated sample(s) lead to the development of a commercial product, the University of South Carolina will own it and may take action to patent and license the product. The University of South Carolina does not intend to provide any compensation for participation in this study nor for any future value that the sample(s) that I have provided may be found to have. I may not receive notice of future uses of my sample(s).

"The purpose and procedures of this research project and the predictable discomfort, risks, and benefits that might result have been explained to me. I have been told that unforeseen events may occur. I have had an opportunity to discuss this with an investigator, and all of my questions have been answered. I agree to participate as a volunteer in this research project being conducted through the Palmetto Health Alliance. I understand that I may end my participation at any time. I understand that there is a possibility that the information I provided, and the tissue samples, which I also provided to this study, may be used in other research studies and could potentially have some commercial applicability. I have been given a copy of this consent form."

IRB APPROVAL

03-19-2004-03-18-2005

Subject's Initials_____

PALMETTO HEALTH ALLIANCE

IRB #2000-69
(No samples required)

Print Name of Participant	Date	Signature of Participant	Date
Print Name of Person Obtaining Consent	Date	Signature of Person Obtaining Consent	Date
Print Name of Witness	Date	Signature of Witness	Date

Participant's permanent address and telephone number:

IRB APPROVAL

03-19-2004 - 03-18-2005

Subject's Initials_____